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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/381,032	12/17/99	BERGMANN	A PM263260

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EXAMINER	
HUYNH, P	
ART UNIT	**PAPER NUMBER**
1644	9

DATE MAILED: 05/04/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/381,032	Applicant(s) BERGMANN ET AL.	
	Examiner " Neon" Phuong Huynh	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. Applicant's election without traverse of Group I, in Paper No. 8, is acknowledged. Because applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
Claims 1-13 are pending.
Claim 13 is withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to non-elected inventions.
Claims 1-12 are being prosecuted in this Office Action.

2. The drawings, filed 12/17/99, are approved.

3. Applicant should amend the first line of the specification to indicate the status of the priority documents, i.e., This application is a 371 of PCT/EP99/00159, filed January 13, 1999. See MPEP 1302.04.

4. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 250 words. It is important that the abstract not exceed 250 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

5. Claims 6-7, 9 and 11 are objected to under 37 CRF 1.75(c) as being in improper form because a **multiple dependent claim** cannot depend from any other multiple dependent claim. See MPEP 608.01(n).

6. The following order or arrangement is preferred in framing the specification and, except for the title of the invention, each of the lettered items should be preceded by the headings indicated below.

(a) Title of the Invention.

(b) cross-references to Related Applications (if any).

(c) Statement as to rights to inventions made under Federally sponsored research and development (if any).

(d) Background of the invention.

1. Field of the Invention.

2. Description of the Related Art including information disclosed under *37 C.F.R. §§ 1.97-1.99.*

(e) Summary of the Invention.

(f) Brief Description of the Drawing.

(g) Description of the Preferred Embodiment(s).

(h) Claim(s).

(i) Abstract of the Disclosure.

7. Appropriate correction is required in the specification. The phrase "The Figures show the following in the form of various diagrams" on page 21 should "Brief Description of the Drawing".

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "**characterized**" as recited in claim 1-12 is indefinite because it is not clear which characteristics are not identifying.

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergmann *et al.* (US Pat No. 5,814,461, filing date July 1996; PTO 892) and or Morris *et al* (J Biol Chem 268(15):10900-5, May 1993; PTO 892) in view of Morgenthaler *et al* (J Clin Endocrinol Metab 81(2):700-6, Feb 1996, PTO 892).

Bergmann *et al* teach a method of detecting autoantibodies to the thyroid stimulating hormone (TSH) receptor in a biological fluid sample (serum) from patient with Graves' disease using a solid phase competitive receptor binding assay (See entire document). The reagents for the method include, test tube as solid phase (See column 7, material and methods in particular), TSH receptor autoantibody from patient serum sample to be measured (See column 9, line 27), porcine TSH receptor as binder (see column 9, line 25 in particular), luminescence labeled bovine or human anti-TSH specific monoclonal antibody as tracer wherein said antibody selectively binds to the free TSH but not the bound TSH (Column 7, line 12; column 9, line 30 in particular), and bovine TSH as competitor (See column 7 line 11 in particular). The TSH specific antibodies include bovine specific monoclonal antibody (See column 7, line 40 in particular) and human TSH specific antibody (See column 7, line 20 in particular). Prior to assay, the luminescence labeled anti-TSH specific monoclonal antibody (tracer) is immobilized to the solid phase, the test tube wherein the receptor binding assay is carried out as a one-step method where TSH antibody is directly labeled (See material and method in particular) or as a two-step method where TSH is

bound to the solid phase and the TSH receptor binding is detected with a labeled second monoclonal anti-TSH antibody (See Fig 1; claims 1 and 5 in particular). The patient sample containing TSH autoantibody is preincubated with the porcine TSH receptor in the presence of bovine TSH competitor (for specific binding), the liquid fraction is then transfer to the test tube that has been coated with anti-TSH specific antibody. After incubation and washing, the displacement of the specific binding of tracer amounts of labeled bovine or human TSH is measured in a manner well known in the art and the amount bTSH detected is proportional to the amount of autoantibodies in the patient sample (See column 9, line 25 and claims in particular). Furthermore, '461 teaches that TSH receptor assays function very much similar to competitive radioimmunoassays where TSH receptors are used as specific binding reagent for autoantibodies and radiolabeled TSH as tracer (See column 3, line 32 bridging column 4 in particular).

Bergmann differs from the claimed invention by immobilizing the labeled TSH specific antibody instead of immobilizing the recombinant human TSH receptor; the bovine TSH receptor is used rather than the recombinant human TSH receptor, and labeled TSH specific antibody was used as tracer for ^{125}I labeled bovine TSH as tracer.

Morris *et al* teach a method of screening synthetic human TSH receptor peptide using an assay which measure the displacement of ^{125}I labeled bovine TSH from binding to the native TSH receptor in the presence of competitor (See entire document; Abstract, Figs 2 and 3, in particular).

Morgenthaler *et al* teach the use of recombinant human TSH receptor for detecting TSH receptor autoantibodies in Graves' disease (See entire document; abstract, in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the recombinant human TSH receptor as taught by Morgenthaler *et al* or Morris *et al* and ^{125}I labeled bovine TSH as tracer as taught by Morris for measuring TSH receptor autoantibodies in Graves' disease by substituting the bovine TSH receptor of '461 with the human TSH receptor as taught by Morgenthaler and Morris and by substituting the labeled bovine TSH antibody of '461 with the ^{125}I labeled bovine TSH as tracer. One having ordinary skill in the art would have been motivated to modify the competitive radioreceptor assays in view of the teachings in each of the secondary references of Morris *et al* that the specific residues of human TSH receptor that are unique in hormone binding have been mapped (See 10901 right column first paragraph, in particular) and Bergmann *et al* that the human anti-TSH receptor autoantibody in Graves' would bind to the human recombinant TSH

receptor with improved specificity and sensitivity over the currently available assays which generally use the porcine TSH receptor (See column 7, line 31, in particular).

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

15. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

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May 2, 2001

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